



purine nucleoside phosphorylase deficiency

Purine nucleoside phosphorylase deficiency is one of several disorders that damage the immune system and cause severe combined immunodeficiency (SCID). People with SCID lack virtually all immune protection from foreign invaders such as bacteria, viruses, and fungi. Affected individuals are prone to repeated and persistent infections that can be very serious or life-threatening. These infections are often caused by "opportunistic" organisms that ordinarily do not cause illness in people with a normal immune system. Infants with SCID typically grow much more slowly than healthy children and experience pneumonia, chronic diarrhea, and widespread skin rashes. Without successful treatment to restore immune function, children with SCID usually do not survive past early childhood.

About two-thirds of individuals with purine nucleoside phosphorylase deficiency have neurological problems, which may include developmental delay, intellectual disability, difficulties with balance and coordination (ataxia), and muscle stiffness (spasticity). People with purine nucleoside phosphorylase deficiency are also at increased risk of developing autoimmune disorders, which occur when the immune system malfunctions and attacks the body's tissues and organs.

Frequency

Purine nucleoside phosphorylase deficiency is rare; only about 70 affected individuals have been identified. This disorder accounts for approximately 4 percent of all SCID cases.

Genetic Changes

Purine nucleoside phosphorylase deficiency is caused by mutations in the *PNP* gene. The *PNP* gene provides instructions for making an enzyme called purine nucleoside phosphorylase. This enzyme is found throughout the body but is most active in specialized white blood cells called lymphocytes. These cells protect the body against potentially harmful invaders by making immune proteins called antibodies that tag foreign particles and germs for destruction or by directly attacking virus-infected cells. Lymphocytes are produced in specialized lymphoid tissues including the thymus and lymph nodes and then released into the blood. The thymus is a gland located behind the breastbone; lymph nodes are found throughout the body. Lymphocytes in the blood and in lymphoid tissues make up the immune system.

Purine nucleoside phosphorylase is known as a housekeeping enzyme because it clears away waste molecules that are generated when DNA is broken down. Mutations in the *PNP* gene reduce or eliminate the activity of purine nucleoside phosphorylase.

The resulting excess of waste molecules and further reactions involving them lead to the buildup of a substance called deoxyguanosine triphosphate (dGTP) to levels that are toxic to lymphocytes. Immature lymphocytes in the thymus are particularly vulnerable to a toxic buildup of dGTP, which damages them and triggers their self-destruction (apoptosis). The number of lymphocytes in other lymphoid tissues is also greatly reduced, resulting in the immune deficiency characteristic of purine nucleoside phosphorylase deficiency.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- nucleoside phosphorylase deficiency
- PNP deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Severe Combined Immunodeficiency (SCID) and Conditions Associated with T Cell Lymphopenia
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/SCID.pdf>

Genetic Testing

- Genetic Testing Registry: Purine-nucleoside phosphorylase deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268125/>

Other Diagnosis and Management Resources

- Baby's First Test: Severe Combined Immunodeficiency
<http://www.babysfirsttest.org/newborn-screening/conditions/severe-combined-immunodeficiency-scid>
- National Marrow Donor Program
<https://bethematch.org/for-patients-and-families/learning-about-your-disease/severe-combined-immunodeficiency/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Immune System and Disorders
<https://medlineplus.gov/immunesystemanddisorders.html>

Genetic and Rare Diseases Information Center

- Purine nucleoside phosphorylase deficiency
<https://rarediseases.info.nih.gov/diseases/4606/purine-nucleoside-phosphorylase-deficiency>

Additional NIH Resources

- National Human Genome Research Institute: Learning About Severe Combined Immunodeficiency
<https://www.genome.gov/13014325/>
- National Institute of Allergy and Infectious Diseases: Primary Immune Deficiency Diseases
<https://www.niaid.nih.gov/diseases-conditions/primary-immune-deficiency-diseases-pids>

Educational Resources

- Disease InfoSearch: Purine nucleoside phosphorylase deficiency
<http://www.diseaseinfosearch.org/Purine+nucleoside+phosphorylase+deficiency/6107>
- MalaCards: immunodeficiency due to purine nucleoside phosphorylase deficiency
http://www.malacards.org/card/immunodeficiency_due_to_purine_nucleoside_phosphorylase_deficiency

- Merck Manual Consumer Version: Severe Combined Immunodeficiency
<http://www.merckmanuals.com/home/immune-disorders/immunodeficiency-disorders/severe-combined-immunodeficiency-scid>
- Orphanet: Purine nucleoside phosphorylase deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=760

Patient Support and Advocacy Resources

- Immune Deficiency Foundation
<http://primaryimmune.org/>
- Jeffrey Modell Foundation
<http://www.info4pi.org/>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22purine+nucleoside+phosphorylase+deficiency%22+OR+%22Severe+Combined+Immunodeficiency%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28purine+nucleoside+phosphorylase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- PURINE NUCLEOSIDE PHOSPHORYLASE DEFICIENCY
<http://omim.org/entry/613179>

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